UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/465,338	12/17/99	ALBERT K	PT-1817

023607 HM12/0504
IVOR M HUGHES
175 COMMERCE VALLEY DRIVE WEST
SUITE 200
THORNHILL ON L3T 7P6
CANADA

AIR MAIL

EXAMINER	
PULLIAM, A	
ART UNIT	**PAPER NUMBER**
1615	14

DATE MAILED: 05/04/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/465,338	ALBERT ET AL.	
	Examiner	Art Unit	
	Amy E Pulliam	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *8,26,54,55 and 61* is/are withdrawn from consideration.

5)☒ Claim(s) *44,46,48,49 and 51* is/are allowed.

6)☒ Claim(s) *1-7,9-25,27-39,41-43,45,47,56-59 and 62* is/are rejected.

7)☒ Claim(s) *40,50,52,53 and 60* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☒ Interview Summary (PTO-413) Paper No(s). *14* .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

DETAILED ACTION

Receipt is acknowledged of the Request for Extension of Time, Request under 37 CFR 1.114, and Amendment C, with attachment, all received April 10, 2001.

Allowable Subject Matter

Claim 40 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 50, 52, 53, and 60 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action.

Claims 44, 46, 48, 49, and 51 are allowed.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17, 18, 35, 36, 50, 52, 53, 56, 57, 59, and 60-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "suitable" in the claims is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining

the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7, 9-25, 27-39, 41-43, 45, 47, 56-59, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over EPA 856 313 to Geoghegan *et al.* ('313).

EPA '313 discloses a controlled absorption diltiazem pellet formulation for oral administration to control hypertension and angina comprising a core of diltiazem or a pharmaceutically acceptable salt thereof, and a multilayer membrane surrounding the core and containing both a water insoluble and a water soluble polymer (abstract). EPA '313 further discloses that the formulation is preferred as a once-daily product to be administered before bedtime, and to be released at the following rates:

a. from 0 to 35% after 2 hours

b. from 4 to 45% after 4 hours

c. from 30 to 75% after 8 hours

d. from 60 to 95% after 13 hours

e. not less than 85% after 24 hours.

These release rates overlap those claimed by applicant in the instant application. Further, EPA '313 teaches that the water insoluble polymer can be replaced by a copolymer of acrylic and methacrylic acid esters (p 28, claim 10), and that the water soluble polymer can be HPMC (p 28, claim 7). EPA '313 also teaches that the core may comprise an organic acid, a lubricant (p 5, l 15-29), and other pharmaceutically acceptable components. In addition, throughout the examples, EPA '313 teaches varying amounts of active ingredient, including 120, 240, and 90 mg. Further, EPA '313 teaches tablet, pellet, and capsule formulations (exs. 8, 14, 21). Although EPA '313 does not disclose the exact release rates claimed by applicant, the ranges claimed fall within the range disclosed by EPA '313, and therefore are rendered obvious by the reference.

EPA '313 does not teach all of the specific amounts of Diltiazem present in the formulation, nor do they teach the specific wetting agent claimed by applicant. However, the formulation disclosed in EPA '313 does teach a varied range of the amount of active ingredient, as well as the presence of additional additives, such as lubricants. Further, the formulation also releases the drug at the same rate as that claimed by applicant, therefore, it appears that these limitations do not render any unexpected results. It is the position of the examiner that these are limitations which would be routinely determined by one of ordinary skill through minimal experimentation, as being suitable, absent the presentation of some unusual and/ or unexpected results. The results must be based on the specific limitations.

Furthermore, it is the position of the examiner that EP '313 teaches the generic concept of the invention, as well as the suggestion to manipulate the formulation to result in varying dissolution rates and Cmax values. One of ordinary skill in the art would have been motivated to manipulate the formulation based on the specifics of the desired formulation. The expected result would be a successful pharmaceutical formulation. Therefore, this invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments have been fully considered but are not found persuasive. Applicant argues that EPA '313 does not have an example which corresponds to applicant's claimed Cmax and release rates. However, as discussed in the last office action, the examiner has pointed out teachings of both applicant's claimed release rates and applicant's claimed Cmax within the prior art reference. Further, as stated above, it is the position of the examiner that EP '313 teaches the generic concept of the invention, as well as the suggestion to manipulate the formulation to result in varying dissolution rates and Cmax values.

Additionally, applicant has submitted data, and claims unexpected results in order to overcome the rejection under 35 U.S.C. 103(a). The examiner has thoroughly considered the submitted data and declarations, and finds them to be persuasive only for a 300 mg capsule, as that is the only dosage form discussed in the comparison. Excluding claim 40, none of the above rejected claims are commensurate in scope with the date provided.

Lastly, applicant argues that the instant invention has unexpected results based on the lower peak to trough variance than the prior art, however, there is nothing in the claim language discussing this limitation.

Claims 1-7, 9-25, 27-39, 41-43, 45, 47, 56-59, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/00093 to Deboeck *et al.* ('093). WO '093 discloses an extended release galenical form of Diltiazem or a pharmaceutically acceptable salt, with a wetting agent, coated with a microporous membrane comprising at least a water soluble polymer and a pharmaceutically acceptable adjuvant. WO '093 further teaches that the composition comprises beads containing between 120 and 480 mg of the active ingredient, with the wetting agent, and the beads are coated with the microporous membrane (p 19, claim 1). WO '093 further teaches that the water soluble polymer or copolymer can include HPMC and Eudragit (p 8, l 21-28). Further, WO '093 teaches that the following ingredients are included in the formulation: wetting agents such as fatty acid esters of saccharose (2-20%), microcrystalline cellulose (5-25%), polyvinylpyrrolidone (1-15%), titanium oxide, surfactants such as tween, antifoaming agents, magnesium stearate, and talc (see pages 8-10). These are the ingredients disclosed by applicant as being present in the formulation. WO '093 also teaches that the formulation is for once daily administration. WO '093 does not teach the exact rates of release as claimed by applicant, nor do they discuss the rates of release after 8 hours, nor do they disclose all of the specific amounts of the above mentioned ingredients. However, WO '093 does teach overlapping rates of release to those

claimed by applicant, and they do teach the same ingredients as claimed by applicant. It is the position of the examiner that the present application is not patentably distinct from WO '093, as they contain the same ingredients, in the same formulation, with overlapping rates of release, even though WO '093 does not disclose the specific amounts of all the ingredients. It is the position of the examiner that the specific amounts of those ingredients which are not disclosed in WO '093 are limitations which would be routinely determined by one of ordinary skill in the art through minimal experimentation, absent the presentation of some unusual and/ or unexpected results. The results must be those that accrue from the specific limitations. Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to create a controlled release formulation of Diltiazem, based on the teachings of WO '093, and experiment with and vary the specific amounts of the ingredients, in order to achieve the desired rate of release.

Applicant argues that WO '093 does not teach the exact Cmax and Tmax as claimed by applicant. The examiner acknowledges this fact, and this is why the WO '093 reference is used as an obviousness reference, not an anticipation reference. It is the position of the examiner that because WO '093 contains the same ingredients in the same formulation, with overlapping release rates, applicant's invention is not patentably distinct from the prior art, therefore, this rejection is maintained.

Furthermore, applicant argues that the peak to trough variance for the WO '093 reference (which corresponds to Tiazac) is much larger than that of applicant's formulation. Applicant has provided evidence to reinforce this statement. However, the

examiner respectfully disagrees as the data regarding Tiazac is concerning a 240 mg formulation, and the data regarding applicant's claimed formulation is based on a 300 mg capsule. Therefore, this comparison is not persuasive, and the rejection is maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E Pulliam whose telephone number is (703) 308-4710. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7922 for regular communications and (703) 308-7922 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Amy E. Pulliam
Patent Examiner
Art Unit 1615
April 30, 2001

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600